

made in a 96-well microtiter plate (Corning Costar 3695) using Solution 1. Following serial dilution each well has 50 μ l of Solution 1. The reaction is started by adding 50 μ l of solution 2 to each well. This may be done with a multichannel pipettor either manually or with automated liquid handling devices. The microtiter plate is then transferred to a microplate absorbance reader and multiple absorbance readings at 340 nm are taken for each well in a kinetic mode. The observed rate of change, which is proportional to the ATPase rate, is then plotted as a function of the compound concentration. For a standard IC_{50} determination the data acquired is fit by the following four parameter equation using a nonlinear fitting program (e.g., Grafit 4):

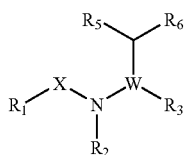
$$y = \frac{\text{Range}}{1 + \left(\frac{x}{IC_{50}}\right)^x} + \text{Background}$$

where y is the observed rate and x the compound concentration.

[1013] Other chemical entities of this class were found to inhibit cell proliferation, although GI_{50} values varied. GI_{50} values for the chemical entities tested ranged from 200 nM to greater than the highest concentration tested. By this we mean that although most of the chemical entities that inhibited mitotic kinesin activity biochemically did inhibit cell proliferation, for some, at the highest concentration tested (generally about 20 μ M), cell growth was inhibited less than 50%. Many of the chemical entities have GI_{50} values less than 10 μ M, and several have GI_{50} values less than 10 μ M. Anti-proliferative compounds that have been successfully applied in the clinic to treatment of cancer (cancer chemotherapeutics) have GI_{50} 's that vary greatly. For example, in A549 cells, paclitaxel GI_{50} is 4 nM, doxorubicin is 63 nM, 5-fluorouracil is 1 μ M, and hydroxyurea is 500 μ M (data provided by National Cancer Institute, Developmental Therapeutic Program, <http://dtp.nci.nih.gov/>). Therefore, compounds that inhibit cellular proliferation at virtually any concentration may be useful.

What is claimed is:

1. At least one chemical entity chosen from compounds of Formula I



Formula I

and pharmaceutically acceptable salts, solvates, chelates, non-covalent complexes, prodrugs, and mixtures thereof, wherein

R_1 is optionally substituted aryl or optionally substituted heteroaryl;

X is $-\text{CO}-$ or $-\text{SO}_2-$;

R_2 is hydrogen or optionally substituted lower alkyl;

W is $-\text{CR}_4-$, $-\text{CH}_2\text{CR}_4-$, or N;

R_3 is $-\text{CO}-R_7$, hydrogen, optionally substituted alkyl, optionally substituted heterocyclyl, cyano, optionally substituted sulfonyl, or optionally substituted aryl;

R_4 is hydrogen or optionally substituted alkyl;

R_5 is hydrogen, hydroxyl, optionally substituted amino, optionally substituted heterocyclyl; or optionally substituted lower alkyl;

R_6 is hydrogen, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted aryloxy, optionally substituted heteraryloxy, optionally substituted alkoxycarbonyl-, optionally substituted aminocarbonyl-, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclyl, or optionally substituted aralkyl; and

R_7 is optionally substituted lower alkyl, optionally substituted aryl, hydroxyl, optionally substituted amino, optionally substituted aralkoxy, or optionally substituted alkoxy;

provided that if W is N, then R_5 is not hydroxyl or optionally substituted amino, and R_6 is not optionally substituted alkoxy, optionally substituted aralkoxy, optionally substituted heteroaralkoxy, or optionally substituted amino.

2. At least one chemical entity of claim 1 wherein R_1 is optionally substituted aryl.

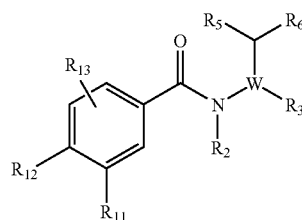
3. At least one chemical entity of claim 2, wherein R_1 is optionally substituted phenyl.

4. At least one chemical entity of claim 3, wherein R_1 is phenyl substituted with one, two or three groups independently selected from optionally substituted heterocyclyl, optionally substituted alkyl, sulfonyl, halo, optionally substituted amino, optionally substituted sulfanyl, optionally substituted alkoxy, optionally substituted aryloxy, optionally substituted heteroaryloxy; acyl, hydroxyl, nitro, cyano, optionally substituted aryl, and optionally substituted heteroaryl-.

5. At least one chemical entity of claim 4, wherein R_1 is 3-halo-4-isopropoxy-phenyl or 3-cyano-4-isopropoxy-phenyl.

6. At least one chemical entity of claim 1 wherein X is $-\text{CO}-$.

7. At least one chemical entity of claim 1 wherein the compound of Formula I is chosen from compounds of Formula II



(Formula II)